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JAMES P. O'HARE, M.D.
BOSTON

Reprinted from the Archives of Internal Medicine
July, 1913, Vol. 12, pp. 49-60

CHICAGO
AMERICAN MEDICAL ASSOCIATION
FIVE HUNDRED AND THIRTY-FIVE NORTH DEARBORN STREET
1913

STUDY XVII: EXPERIMENTAL CHRONIC NEPHRITIS PRODUCED BY THE COMBINATION OF CHEMICAL (URANIUM NITRATE) AND BACTERIA (*B. COLI COMMUNIS*)*

JAMES P. O'HARE, M.D.
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This study has been made at the suggestion of Dr. Henry A. Christian in an attempt to produce a chronic nephritis in animals in a manner comparable to that used by Opie[1] in the production of an experimental cirrhosis of the liver. Opie found that repeated injections of chloroform, which causes a necrosis of the liver, and *Bacillus coli communis,* whose relation to the liver is quite intimate, produced a well-marked sclerosis of the liver. In the present experiments repeated injections of uranium nitrate and *B. coli communis* were made in rabbits to see if in similar way a sclerosis of the kidney would be produced. Uranium nitrate is known to produce an acute nephritis similar to that occurring in human beings in which there is very extensive necrosis of the tubular epithelium, and has been shown by Dickson,[2] Smith[3] and others, to produce a chronic nephritis when injected repeatedly over a long period of time. Although the relationship between *B. coli communis* and the kidney is not as intimate as that with the liver, infection of the urinary tract with colon bacilli is fairly common and it has been suggested that these bacteria may play a part in the chronic nephritis occurring in man.

Rabbits were the animals used. Although full grown rabbits were selected in most of the experiments, it was found very difficult to keep them alive long enough to produce any chronic lesion. In fact, about one-half of all the rabbits started, died within a few days, either from a septicemia from *B. coli communis* or from the uranium nitrate, or from both. Only eighteen out of forty rabbits used, survived long enough to produce any chronic lesions. These eighteen were carried through a

* A series of studies on experimental cardiovascular disease has been published previously; see Study XVI, THE ARCHIVES OF INT. MED., 1913, xi, 517, for reference to these.

* From the Laboratory of the Department of the Theory and Practice of Physic, Medical School, Harvard University.

* This work was done under a grant from the Proctor Fund for the Study of Chronic Diseases.

* Submitted for publication March 25, 1913.

1. Opie: Jour. Exper. Med., 1909, xii, 237.
2. Dickson: THE ARCHIVES INT. MED., 1909, iii, 375.
3. Smith: THE ARCHIVES INT. MED., 1911, viii, 481.

period of life varying from a few weeks to five months. Some died, most of them were killed.

The exact method employed varied with the individual animal and can be found in the protocols. One was given 5 mg. of uranium nitrate subcutaneously every three weeks, and at the same time 0.25 c.c. of a twenty-four hour bouillon culture of *B. coli communis* intravenously every three days. Four were given 2 mg. uranium nitrate at intervals of three days for three doses, followed by three doses of 0.25 c.c. of a twenty-four hour bouillon culture of *B. coli communis* at three-day intervals, etc. The rest were given alternate doses of uranium nitrate 2 mg., and *B. coli communis* 0.25 c.c. at three-day intervals. In one



Fig. 1.—Rabbit 370. Magnification 65 diameters. Kidney showing area of connective tissue increase radiating into the cortex from the surface.

case, Rabbit 370, the dose of *B. coli communis* was increased during the last two months to 0.35 c.c.

The results of this treatment were that twelve out of the eighteen rabbits showed a moderately marked increased of the connective tissue, four a moderate increase, two a slight increase in the connective tissue. In thirteen the connective tissue was present in the outer cortex, usually starting from the surface in form of a scar running down one or more of the rays. (Fig. 1, Rabbit 370; Fig. 2, Rabbit 445; Fig. 3, Rabbit 461; Fig. 4, Rabbit 472.) In two of these cases the connective tissue was very marked in the outer cortex. In seventeen of the cases there was increased

fibrous tissue at the junction between the cortex and the medulla. (Fig. 5, Rabbit 471; Fig. 6, Rabbit 473; Fig. 7, Rabbit 460.) This seemed to be the favorite place for the greatest increase, as thirteen of the eighteen cases showed a marked increase in this region. Fourteen cases showed an increase of fibrous tissue in the medulla; in none was the increase very marked.

The connective tissue was quite fibrous in most cases, though in some it was faily cellular. In most of the kidneys all three localities were involved, the connective tissue spreading from the surface down the rays in form of scars containing distorted glomeruli. These scars were con-



Fig. 2.—Rabbit 445. Magnification 65 diameters. Kidney showing area of connective tissue increase radiating into the cortex from the surface.

nected at the apex of the labyrinths by a thick band of connective tissue running parallel to the surface. The connective tissue in the medulla was never very marked.

Lymphocytic infiltration was present in ten of the eighteen cases, but was well marked in only three of the cases. No special part of the kidney was singled out, clumps of small lymphocytes being present here and there in all parts.

Most of the cases showed involvement of the glomeruli, this taking one or more of several forms. Ten showed distinct drawing together of the glomeruli by contraction of the connective tissue in the scars. (Figs.

1, 2 and 3.) Six showed a more or less marked dilatation of the capsule, usually accompanied by a shrinking of the tuft as from pressure of fluid in the capsular space. (Fig. 3.) Five showed shrinking of the glomeruli and twelve a distinct thickening of the capsular walls of many glomeruli. Ten showed also a thickening of the walls of the vessels in the tuft. Four showed a proliferation of the endothelial cells in the glomeruli and four an increased number of red blood-corpuscles in the glomeruli. Only seven out of the eighteen showed any dilatation of tubules such as Smith[3] speaks about. This is only well marked in two cases. (Fig. 8, Rabbit 442.)

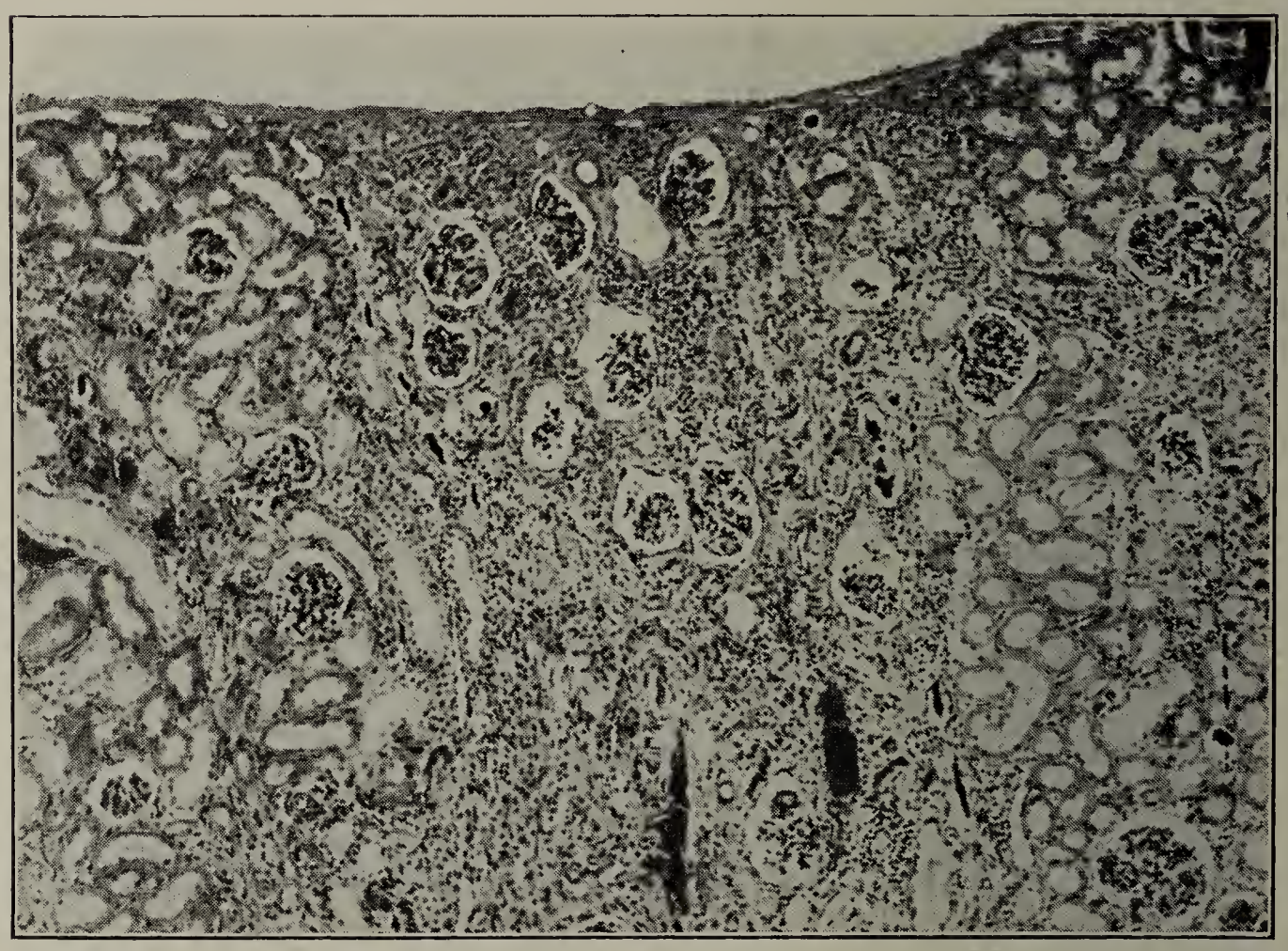


Fig. 3.—Rabbit 461. Magnification 65 diameters. Kidney showing area of connective tissue increase radiating into the cortex from the surface.

In comparing the results of this series of experiments with those obtained by Smith[3] a general impression was obtained that chronic changes were more regularly encountered in the kidneys of rabbits which had received both uranium nitrate and *Bacillus coli communis* than in those rabbits which had received only uranium nitrate. It was found difficult, however, to make an actual comparison between the lesions in two sets, inasmuch as the rabbits of Smith's series of experiments varied considerably in the method of treatment from the rabbits in this series, both with regard to the dosage and the time elapsing between the last dose and the time of death.

There were, however, ten rabbits which were carried through an approximately equal period of active treatment. In five uranium nitrate alone was given; in the other five alternate doses of uranium nitrate and *Bacillus coli communis* were given, the total number of doses of the two being approximately the same as the total number of doses of uranium nitrate in the first five. In these rabbits the amount of connective tissue change showed no great preponderance in either set. On the whole, the connective tissue was rather more dense in the kidneys of the rabbits which had received both uranium nitrate and *Bacillus coli communis.* In addition to these ten rabbits, there were six rabbits, all of which had

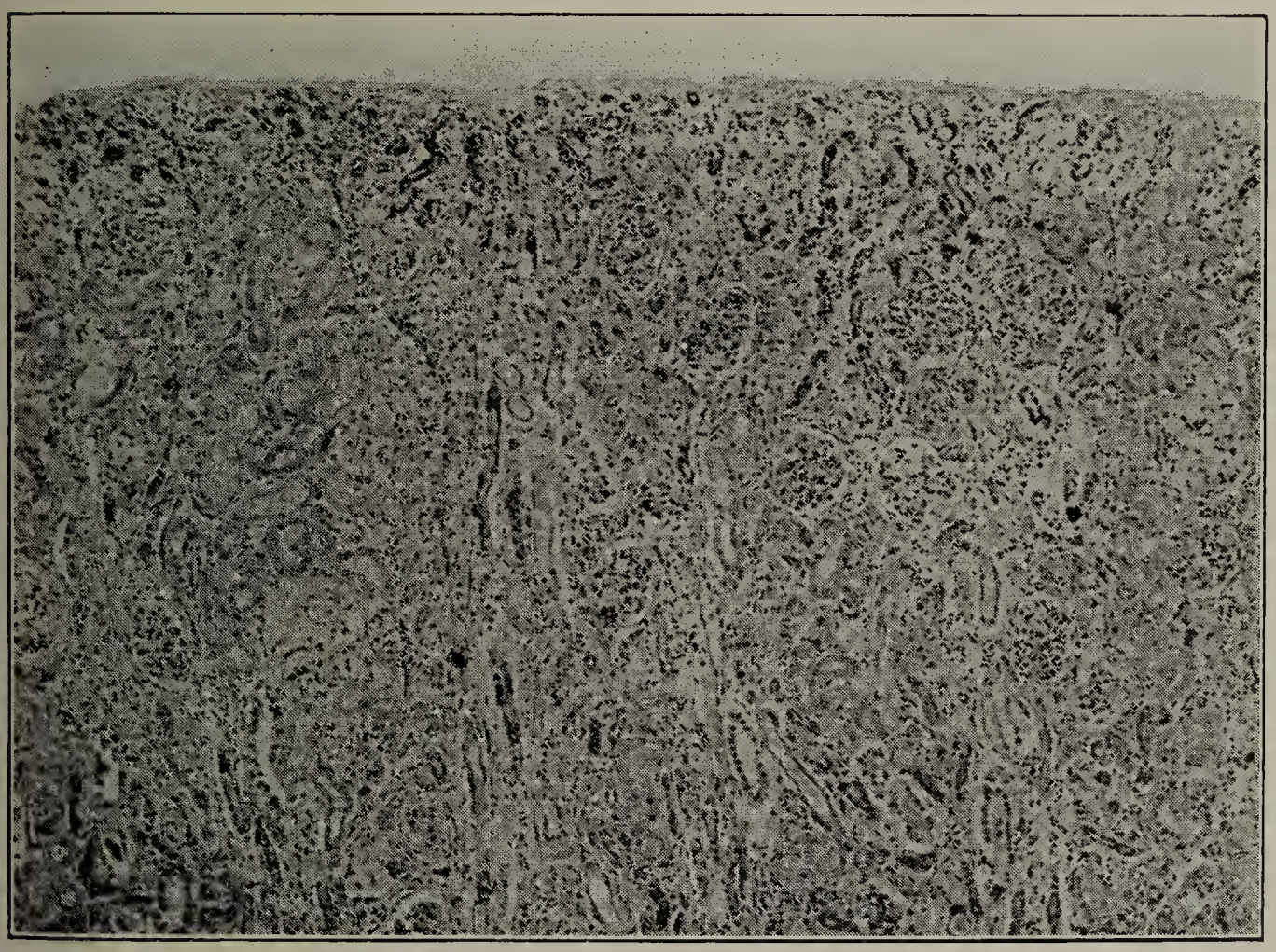


Fig. 4.—Rabbit 472. Magnification 65 diameters. Kidney showing area of connective tissue increase radiating into the cortex from the surface.

received approximately the same number of equal size doses of uranium nitrate over a period of equivalent time. Three of these in addition had received doses of *Bacillus coli communis.* In this set the rabbits that had received both uranium nitrate and *Bacillus coli communis* showed distinctly a more marked connective tissue change in their kidneys.

In any study of experimental chronic nephritis in the rabbit it must be kept in mind that the kidney of the rabbit very frequently shows a slight amount of connective tissue which has arisen under natural conditions in the animal, and is not the result of any form of experimental treatment. Occasionally quite marked chronic lesions are encountered

in these untreated animals. Making due allowance for these spontaneous lesions and utilizing as controls the tissues of the kidneys of those rabbits in the series which died of acute lesions very shortly after the beginning of the treatment, it would appear that the combination of uranium nitrate and *Bacillus coli communis* very definitely and quite regularly produces in the rabbit's kidney a chronic lesion with connective tissue increase, and other changes in many respects comparable to the lesions of chronic interstitial nephritis in man in so far as renal elements are concerned. The arteriosclerotic lesions that are so common in the human kidneys of chronic interstitial nephritis are not found in these rabbit kidneys.



Fig. 5.—Rabbit 471. Magnification 65 diameters. Kidney showing connective tissue increase at the junction between cortex and medulla.

In the series of kidneys described in this paper it would seem fair to exclude those kidneys described as showing a moderate or slight increase in connective tissue change, inasmuch as these changes, though rather more frequent in this series, were not in excess of the lesions very commonly found in untreated rabbits. This, then, would leave twelve rabbits in which a considerable increase in connective tissue was produced in the kidney after injections of uranium nitrate and *Bacillus coli communis* covering a very considerable period of time as shown in the protocols. In other words, of 40 rabbits used in these experiments, 22 died so soon after the first injections as to exclude the possibility of any

chronic lesion; 18 lived long enough under treatment to show possible chronic lesions. Of these 18, 12 or two-thirds, showed a considerable degree of chronic change, sufficient to justify the term chronic experimental nephritis. The remaining 6, though showing some chronic change, are excluded from the series inasmuch as the change shown was not more than is frequently seen in rabbits not treated.

The protocols of the rabbits showing more definite changes are appended.

PROTOCOLS

Rabbit 366.—Weight, 1,650 grams. Uranium nitrate subcutaneously 3 mg., Dec. 4, 1911; 5 mg., December 9; 3 mg., December 11; 5 mg., December 13. *B. coli communis* intravenously 0.25 c.c. of 24-hour bouillon culture, December

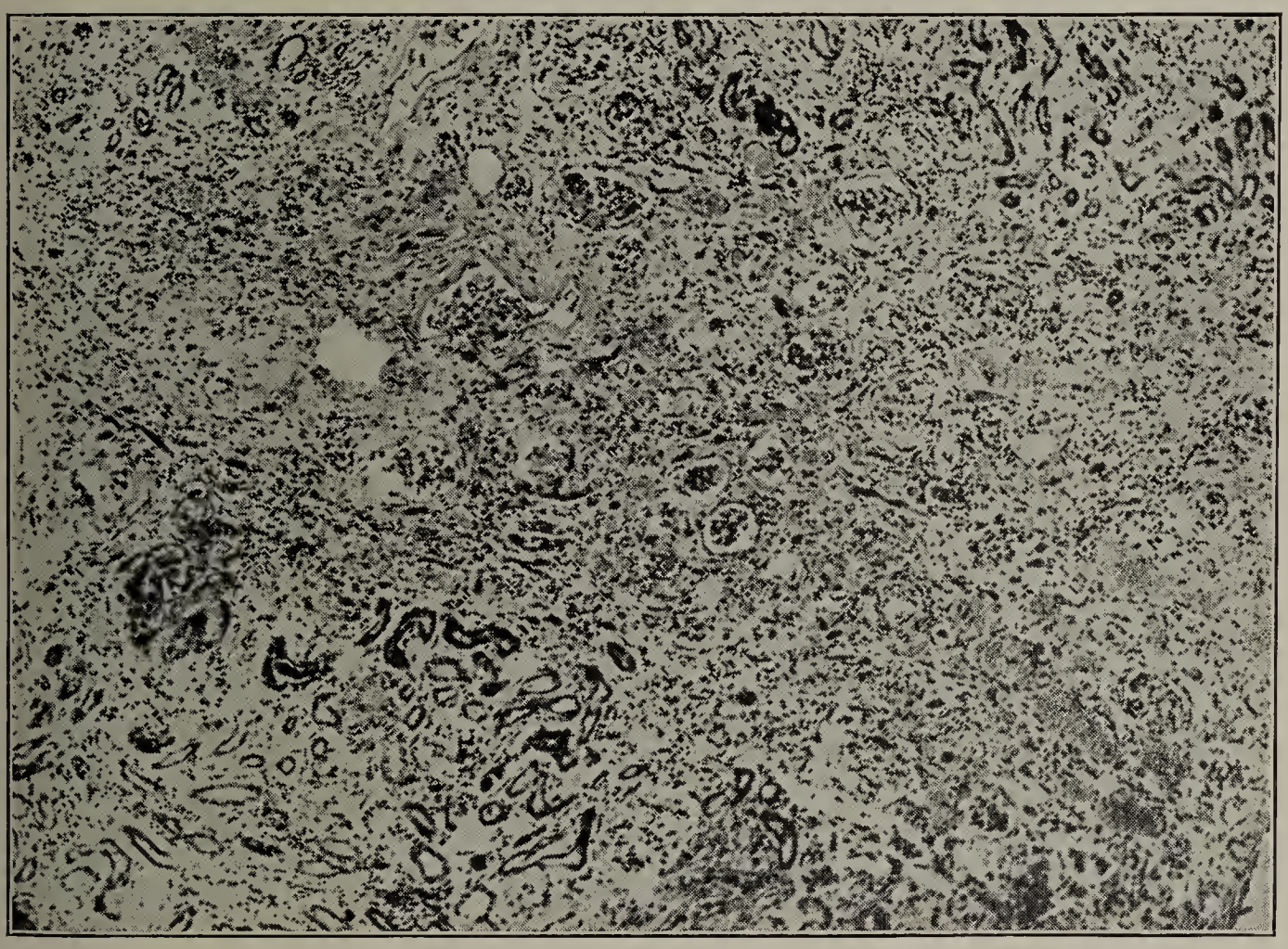


Fig. 6.—Rabbit 473. Magnification 65 diameters. Kidney showing connective tissue increase at the junction between cortex and medulla.

15, 18, 21. Uranium nitrate subcutaneously 2 mg., December 24, 27, 30. *B. coli communis* intravenously 0.25 c.c., Jan. 2, 5, 8, 1912. Uranium nitrate subcutaneously 2 mg., January 11, 14, 17. *B. coli communis* intravenously 0.25 c.c., January 20, 23, 26. Uranium nitrate subcutaneously 2 mg., January 29, February 1, 4. *B. coli communis* intravenously 0.25 c.c., February 7, 10, 13. Uranium nitrate 2 mg. subcutaneously, February 16, 19, 22. *B. coli communis* intravenously 0.35 c.c., February 25, 28, March 2. Uranium nitrate subcutaneously 2 mg., March 5, 7, 10.

Rabbit killed March 12, 1912. Duration of experiment seventy days. Kidney shows moderate connective tissue increase most marked in mid-zonal region.

Rabbit 370.—Caged Dec. 21, 1911. Urine negative. Uranium nitrate subcutaneously 2 mg., December 22, 24, 27, 30. *B. coli communis* intravenously 0.25 c.c. of 24-hour bouillon culture, Jan. 2, 5, 8, 1912. Uranium nitrate sub-

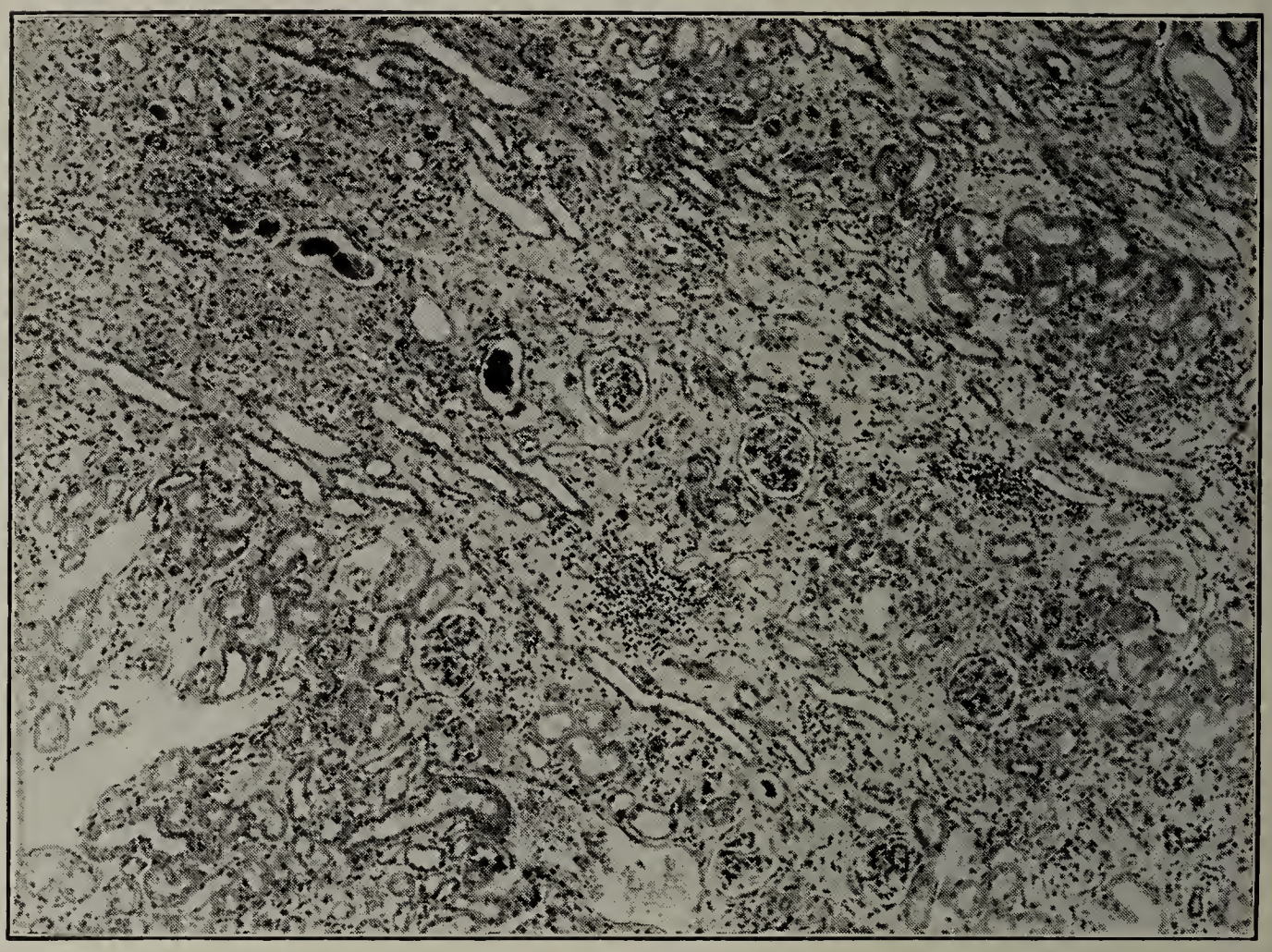


Fig. 7.—Rabbit 460. Magnification 65 diameters. Kidney showing connective tissue increase at the junction between cortex and medulla.



Fig. 8.—Rabbit 442. Magnification 65 diameters. Kidney showing connective tissue radiating into the cortex from the surface with dilatation of adjacent renal tubules.

cutaneously 2 mg., Jan. 11, 14, 17. *B. coli communis* intravenously 0.25 c.c., January 20, 23, 26. Uranium nitrate subcutaneously 2 mg., Jan. 29, February 1, 4. *B. coli communis* intravenously 0.25 c.c., February 7, 10, 13. Uranium nitrate subcutaneously 2 mg., February 16, 19, 22. *B. coli communis* intravenously 0.35 c.c., February 25, 28, March 2. Uranium nitrate subcutaneously 2 mg., March 5, 7, 10. *B. coli communis* intravenously 0.35 c.c., March 15, 18, 21. Uranium nitrate subcutaneously 2 mg., March 24, 27, 30. *B. coli communis* intravenously 0.35 c.c., April 2, 5, 8. Uranium nitrate subcutaneously 2 mg., April 11, 14, 17. *B. coli communis* intravenously 0.35 c.c., April 21.

Killed April 24, 1912. Duration of experiment 126 days. Kidney shows bands radiating in from the surface in which there is a moderate connective tissue increase, rather cellular in character.

Rabbit 382.—Weight, 1,400 grams. Caged Dec. 28, 1911. Urine negative. Uranium nitrate subcutaneously 3.33 mg. per K., December 30, 31. *B. coli communis* intravenously 0.25 c.c. of a 24-hour bouillon culture, January 27. Uranium nitrate subcutaneously 5 mg., February 17. *B. coli communis* intravenously 0.25 c.c., March 9. Uranium nitrate subcutaneously 5 mg. and *B. coli communis* intravenously 0.25 c.c., March 30. *B. coli communis* intravenously 0.25 c.c., April 2, 5, 8, 11, 14, 18. Uranium nitrate subcutaneously 5 mg. and *B. coli communis* intravenously 0.25 c.c., April 21. *B. coli communis* intravenously 0.25 c.c., April 24, 27, 30, May 4, 7, 10, 13, 15, 17, 20, 23, 26, 29, June 1. Uranium nitrate subcutaneously 5 mg. and *B. coli communis* intravenously 0.25 c.c., June 4. *B. coli communis* intravenously 0.25 c.c., June 7.

Killed June 10, 1912. Duration of experiment 165 days. Kidney shows condition quite similar to Rabbit 366.

Rabbit 440.—Caged March 3, 1912. Urine negative. Uranium nitrate subcutaneously 2 mg., March 24. *B. coli communis* intravenously 0.25 c.c., of 24-hour bouillon culture, March 27. Uranium nitrate subcutaneously 2 mg., March 30. *B. coli communis* intravenously 0.25 c.c., April 2. Uranium nitrate subcutaneously 2 mg., April 5. *B. coli communis* intravenously 0.25 c.c., April 14. Uranium nitrate subcutaneously 2 mg., April 18. *B. coli communis* intravenously 0.25 c.c, April 21. Uranium nitrate subcutaneously 2 mg., April 24. *B. coli communis* intravenously 0.25 c.c., April 27. Uranium nitrate subcutaneously 2 mg., April 30. *B. coli communis* intravenously 0.25 c.c., May 24. Uranium nitrate subcutaneously 2 mg., May 7. *B. coli communis* intravenously 0.25 c.c., May 10. Uranium nitrate subcutaneously 2 mg., May 13. *B. coli communis* intravenously 0.25 c.c., May 17. Uranium nitrate subcutaneously 2 mg., May 20. *B. coli communis* intravenously 0.25 c.c., May 23. Uranium nitrate subcutaneously 2 mg., May 26. *B. coli communis* intravenously 0.25 c.c., May 29. Uranium nitrate subcutaneously 2 mg., June 1. *B. coli communis* intravenously 0.25 c.c., June 4. Uranium nitrate subcutaneously 2 mg., June 7. *B. coli communis* intravenously 0.25 c.c., June 10. Uranium nitrate subcutaneously 2 mg., June 13. *B. coli communis* intravenously 0.25 c.c, June 16, etc. *B. coli communis* intravenously 0.25 c.c., June 26.

Killed July 8, 1912. Duration of experiment 106 days. Kidney shows slight focal increase in connective tissue, cellular in type.

Rabbit 442.—Weight, 1,560 grams. Caged March 9, 1912. Urine negative. Uranium nitrate subcutaneously 2 mg., March 10, 13, 16. *B. coli communis* intravenously 0.25 c.c. of a 24-hour bouillon culture, March 18, 21, 24. Uranium nitrate subcutaneously 2 mg., March 27, 30, April 2. *B. coli communis* intravenously 0.25 c.c., April 5, 8, 11. Uranium nitrate subcutaneously 2 mg., April 14, 17, 21. *B. coli communis* intravenously 0.25 c.c., April 24, 27, 30. Uranium nitrate subcutaneously 2 mg., May 4, 7, 10. *B. coli communis* intravenously 0.25

c.c., May 13, 17, 20. Uranium nitrate subcutaneously 2 mg., May 23, 26, 29. *B. coli communis* intravenously June 1, 4, 7.

Killed June 10, 1912. Duration of experiment 93 days. Kidney shows scattered areas of connective tissue increase with distinct dilatation of some of tubules.

Rabbit 445.—Weight, 1,530 grams. Caged March 10, 1912. Urine negative. Uranium nitrate subcutaneously 2 mg., March 11, 14, 16. *B. coli communis* intravenously 0.25 c.c. of a 24-hour bouillon culture, March 18, 21, 24. Uranium nitrate subcutaneously 2 mg., March 27, 30, April 2. *B. coli communis* intravenously 0.25 c.c., April 5, 8, 11. Uranium nitrate subcutaneously 2 mg., April 14, 17, 21. *B. coli communis* intravenously 0.25 c.c., April 24, 27, 30. Uranium nitrate subcutaneously 2 mg., May 4, 7, 10. *B. coli communis* intravenously 0.25 c.c., May 13, 17, 20. Uranium nitrate subcutaneously 2 mg., May 23, 26, 29. *B. coli communis* intravenously 0.25 c.c., June 1, 4, 7.

Killed June 10, 1912. Duration of experiment 92 days. Kidney shows quite large areas in which there is a very considerable connective tissue increase.

Rabbit 460.—Weight, 2,380 grams. Caged March 27, 1912. Urine negative. Uranium nitrate subcutaneously 2 mg., March 27. *B. coli communis* intravenously 0.25 c.c. of 24-hour bouillon culture, March 30. Uranium nitrate subcutaneously 2 mg., April 2. *B. coli communis* intravenously 0.25 c.c., April 5. Uranium nitrate subcutaneously 2 mg., April 8. *B. coli communis* intravenously 0.25 c.c., April 11. Uranium nitrate subcutaneously 2 mg., April 14. *B. coli communis* intravenously 0.25 c.c., April 17. Uranium nitrate subcutaneously 2 mg., April 21. *B. coli communis* intravenously 0.25 c.c., April 24. Uranium nitrate subcutaneously 2 mg., April 27. *B. coli communis* intravenously 0.25 c.c., April 30. Uranium nitrate subcutaneously 2 mg., May 4. *B. coli communis* intravenously 0.25 c.c., May 7. Uranium nitrate subcutaneously 2 mg., May 10. *B. coli communis* intravenously 0.25 c.c., May 13. Uranium nitrate subcutaneously 2 mg., May 17. *B. coli communis* intravenously 0.25 c.c., May 20. Uranium nitrate subcutaneously 2 mg., May 23. *B. coli communis* intravenously 0.25 c.c., May 26. Uranium nitrate subcutaneously 2 mg., May 29. *B. coli communis* intravenously 0.25 c.c., June 1. Uranium nitrate subcutaneously 2 mg., June 16. *B. coli communis* intravenously 0.25 c.c., June 20. Uranium nitrate subcutaneously 2 mg., June 23. *B. coli communis* intravenously 0.25 c.c., June 26. Uranium nitrate subcutaneously 2 mg., June 29.

Killed July 8, 1912. Duration of experiment 103 days. Kidney shows picture quite similar to Rabbit 445.

Rabbit 461.—Weight, 2,100 grams. Caged March 27, 1912. Urine negative. Uranium nitrate subcutaneously 2 mg., March 27. *B. coli communis* intravenously 0.25 c.c. of 24-hour bouillon culture, March 30. Uranium nitrate subcutaneously 2 mg., April 2. *B. coli communis* intravenously 0.25 c.c., April 5. Uranium nitrate subcutaneously 2 mg., April 8. *B. coli communis* intravenously 0.25 c.c., April 11. Uranium nitrate subcutaneously 2 mg., April 14. *B. coli communis* intravenously 0.25 c.c., April 18. Uranium nitrate intravenously 2 mg., April 21. *B. coli communis* intravenously 0.25 c.c., April 24. Uranium nitrate subcutaneously 2 mg., April 27. *B. coli communis* intravenously 0.25 c.c., April 30. Uranium nitrate subcutaneously 2 mg., May 4. *B. coli communis* intravenously 0.25 c.c., May 7. Uranium nitrate subcutaneously 2 mg., May 10. *B. coli communis* intravenously 0.25 c.c., May 13. Uranium nitrate subcutaneously 2 mg., May 17. *B. coli communis* intravenously 0.25 c.c., May 20. Uranium nitrate subcutaneously 2 mg., May 23. *B. coli communis* intravenously 0.25 c.c., May 26. Uranium nitrate subcutaneously 2 mg., May 29. *B. coli communis* intravenously 0.25 c.c., June 1. Uranium nitrate subcutaneously 2 mg., June 4. *B. coli communis* intravenously 0.25 c.c., June 7. Uranium nitrate subcutaneously 2 mg., June 10. *B. coli communis* intravenously 0.25 c.c., June 13. Uranium nitrate subcutaneously 2 mg., June 16. *B. coli communis* intravenously 0.25 c.c., June 20. Uranium nitrate subcutaneously 2 mg., June 23. *B. coli*

communis intravenously 0.25 c.c., June 26. Uranium nitrate subcutaneously 2 mg., June 29.

Killed July 8, 1912. Duration of experiment ninety-eight days. Kidney shows areas radiating in from surface in which there is considerable connective tissue increase, cellular in character with almost complete disappearance of tubules.

RABBIT 468.—Weight, 1,890 grams. Caged April 10, 1912. Urine negative. Uranium nitrate subcutaneously 2 mg., April 11. *B. coli communis* intravenously 0.25 c.c. of 24-hour bouillon culture, April 14. Uranium nitrate subcutaneously 2 mg., April 18. *B. coli communis* intravenously 0.25 c.c., April 21. Uranium nitrate subcutaneously 2 mg., April 24. *B. coli communis* intravenously 0.25 c.c., April 27. Uranium nitrate subcutaneously 2 mg., April 30. *B. coli communis* intravenously 0.25 c.c., May 4. Uranium nitrate subcutaneously 2 mg., May 7. *B. coli communis* intravenously 0.25 c.c., May 10. Uranium nitrate subcutaneously 2 mg., May 13. *B. coli communis* intravenously 0.25 c.c., May 17. Uranium nitrate subcutaneously 2 mg., May 20. *B. coli communis* intravenously 0.25 c.c., May 23. Uranium nitrate subcutaneously 2 mg., May 26. *B. coli communis* intravenously 0.25 c.c., May 29. Uranium nitrate subcutaneously 2 mg., June 1. *B. coli communis* intravenously 0.25 c.c., June 4. Uranium nitrate subcutaneously 2 mg., June 7. *B. coli communis* intravenously 0.25 c.c., June 10. Uranium nitrate subcutaneously 2 mg., June 13. *B. coli communis* intravenously 0.25 c.c., June 16. Uranium nitrate subcutaneously 2 mg., June 20. *B. coli communis* intravenously 0.25 c.c., June 23. Uranium nitrate subcutaneously 2 mg., June 26. *B. coli communis* intravenously 0.25 c.c., June 29.

Killed July 8, 1912. Duration of experiment 89 days. Kidney shows moderate degree of connective tissue increase, more marked in mid-zonal region and fairly cellular.

RABBIT 470.—Weight, 1,820 grams. Caged April 10, 1912. Urine negative. Uranium nitrate subcutaneously 2 mg., April 11. *B. coli communis* intravenously 0.25 c.c., of 24-hour bouillon culture, April 14. Uranium nitrate subcutaneously 2 mg., April 17. *B. coli communis* intravenously 0. 25 c.c., April 21. Uranium nitrate subcutaneously 2 mg., April 24. *B. coli communis* intravenously 0.25 c.c., April 27. Uranium nitrate subcutaneously 2 mg., April 30. *B. coli communis* intravenously 0.25 c.c., May 4. Uranium nitrate subcutaneously 2 mg., May 7, etc., to June 10.

Found dead June 10, 1912. Duration of experiment fifty-nine days. Kidney shows a moderate degree of connective tissue increase quite diffuse in its distribution.

RABBIT 471.—Weight, 1,912 grams. Caged April 10, 1912. Urine negative. Uranium nitrate subcutaneously 2 mg., April 11. *B. coli communis* intravenously 0.25 c.c. of 24-hour bouillon culture, April 14. Uranium nitrate subcutaneously 2 mg., April 17. *B. coli communis* intravenously 0.25 c.c., April 21. Uranium nitrate subcutaneously 2 mg., April 24. *B. coli communis* intravenously 0.25 c.c., April 27. Uranium nitrate subcutaneously 2 mg., April 30. *B. coli communis* intravenously 0.25 c.c., May 4. Uranium nitrate subcutaneously 2 mg., May 7. *B. coli communis* intravenously 0.25 c.c., May 10. Uranium nitrate subcutaneously 2 mg., May 13. *B. coli communis* intravenously 0.25 c.c., May 17. Uranium nitrate subcutaneously 2 mg., May 20. *B. coli communis* intravenously 0.25 c.c., May 23. Uranium nitrate subcutaneously 2 mg., May 26. *B. coli communis* intravenously 0.25 c.c., May 29. Uranium nitrate subcutaneously 2 mg., June 1. *B. coli communis* intravenously 0.25 c.c., June 4. Uranium nitrate subcutaneously 2 mg., June 7. *B. coli communis* intravenously 0.25 c.c., June 10. Uranium nitrate subcutaneously 2 mg., June 13. *B. coli communis* intravenously 0.25 c.c., June 16.

Found dead June 20, 1912. Duration of experiment sixty-nine days. Kidney shows condition quite similar to Rabbit 470, but more marked in degree.

RABBIT 472.—Weight, 1,450 grams. Caged April 7, 1912. Urine negative. Uranium nitrate subcutaneously 2 mg., April 11. *B. coli communis* intravenously 0.25 c.c. of 24-hour bouillon culture, April 14. Uranium nitrate subcutaneously 2 mg., April 18. *B. coli communis* intravenously 0.25 c.c., April 21. Uranium nitrate subcutaneously 2 mg., April 24. *B. coli communis* intravenously 0.25 c.c., April 27. Uranium nitrate subcutaneously 2 mg., April 20. *B. coli communis* intravenously 0.25 c.c., May 4. Uranium nitrate subcutaneously 2 mg., May 7. *B. coli communis* intravenously 0.25 c.c., May 10. Uranium nitrate subcutaneously 2 mg., May 13. *B. coli communis* intravenously 0.25 c.c., May 17. Uranium nitrate subcutaneously 2 mg., May 20. *B. coli communis* intravenously 0.25 c.c., May 23. Uranium nitrate subcutaneously 2 mg., May 26. *B. coli communis* intravenously 0.25 c.c., May 29. Uranium nitrate subcutaneously 2 mg., June 1. *B. coli communis* intravenously 0.25 c.c., June 4.

Found dead June 5, 1912. Duration of experiment fifty-four days. Kidney shows condition quite similar to Rabbit 471.

RABBIT 473.—Caged April 20, 1912. Urine negative. Uranium nitrate subcutaneously 2 mg., April 21. *B. coli communis* intravenously 0.25 c.c. of 24-hour bouillon culture, April 24. Uranium nitrate subcutaneously 2 mg., April 27. *B. coli communis* intravenously 0.25 c.c., April 30. Uranium nitrate subcutaneously 2 mg., May 4. *B. coli communis* intravenously 0.25 c.c., May 7. Uranium nitrate subcutaneously 2 mg., May 10. *B. coli communis* intravenously 0.25 c.c., May 13. Uranium nitrate subcutaneously 2 mg., May 17. *B. coli communis* intravenously 0.25 c.c., May 20. Uranium nitrate subcutaneously 2 mg., May 23. *B. coli communis* intravenously 0.25 c.c., May 26. Uranium nitrate subcutaneously 2 mg., May 29. *B. coli communis* intravenously 0.25 c.c, June 1. Uranium nitrate subcutaneously 2 mg., June 4. *B. coli communis* intravenously 0.25 c.c., June 7. Uranium nitrate subcutaneously 2 mg., June 10. *B. coli communis* intravenously 0.25 c.c., June 13. Uranium nitrate subcutaneously 2 mg., June 16. *B. coli communis* intravenously 0.25 c.c., June 20.

Found dead June 21, 1912. Duration of experiment sixty-three days. Kidney shows quite marked connective tissue increase, diffuse in character and in addition areas of marked connective tissue increase radiating in from surface in which tubules have practically disappeared.

CONCLUSIONS

In rabbits that survive the immediate toxic effects of the agents employed, chronic renal lesions can be produced with considerable regularity by injections of a chemical (uranium nitrate) and a bacteria (*B. coli communis*). The lesions so produced are closely similar to those involving the renal tissues in chronic interstitial nephritis in man.

Carney Hospital.